


# Erythema multiforme following exposure to the herbicide atrazine

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## ABSTRACT

Erythema multiforme is an acute hypersensitivity eruption with sharply demarcated papules and plaques. It has many known causes, from herpes simplex virus and drugs to malignancy and environmental factors. Although other herbicides have been linked to erythema multiforme, no previous reports have described a link with atrazine. We present a 24-year-old man with difficulty breathing, bilateral eye pain with redness, and a diffuse rash consistent with erythema multiforme following occupational exposure to atrazine.

**KEYWORDS** Clinical dermatology; erythema multiforme; herbicide

Erythema multiforme is an acute, self-limiting, inflammatory skin eruption with many known causes, most commonly infectious agents and drugs. Less common causes include malignancy, environmental factors, autoimmune disease, and vaccinations.<sup>1</sup> There have been a few reports of erythema multiforme resulting from exposure to the herbicides paraquat, glyphosphate, alachlor, and butachlor, but no reports discussing an erythema multiforme reaction to the herbicide atrazine.<sup>2–5</sup> We present a case of erythema multiforme caused by atrazine, or 1-chloro-3-ethylamino-5-isopropylamino-2,4,6-triazine.

## CASE REPORT

A 24-year-old man presented to the emergency department with a 3-day history of worsening throat pain, difficulty swallowing, and bilateral eye pain with redness. Five days earlier, he sprayed Weed and Feed fertilizer and herbicide containing 1.5% atrazine. He worked as a landscaper but had not previously worked with this chemical. The following morning, he presented to an acute care facility with throat pain and was thought to have the flu. He was discharged with antibiotics and oseltamivir. The next day he presented to the same facility with a diffuse rash, difficulty breathing, and a fever of 102.7°F. He was transferred to our facility where he required intubation and was admitted for further workup and management.

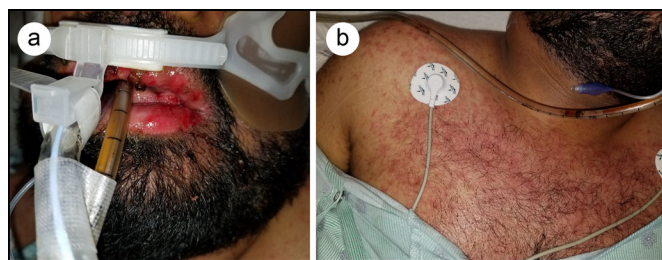
The patient had been on lisinopril for a year for hypertension. He denied any previous episodes of a similar rash and had no known drug or environmental allergens. Physical exam showed multiple erythematous papules, plaques, and patches involving the face, chest, shoulders, and upper back (*Figure 1*), with involvement of 25% body surface area. The palms had ill-defined erythematous macules. There were erosions with hemorrhagic crust on both the lips and the glans penis, as well as conjunctivitis with a purulent discharge. Radiological imaging showed diffuse swelling of the oropharynx and hypopharynx, which were completely occluded except for the endotracheal tube. Additionally, computed tomography of the chest revealed nearly complete opacification of the right lung.

The patient underwent bronchoscopy with bronchial alveolar lavage for right lung collapse. On cytology, no malignancy or viral changes were seen, and there was no growth on fungal or acid-fast bacilli culture after 2 weeks. The patient tested negative by polymerase chain reaction for cytomegalovirus, herpes simplex virus, and varicella-zoster virus. A punch biopsy from a lesion on the left chest revealed necrotic keratinocytes with early bullae formation. Together with the patient's history and clinical presentation, this finding was most consistent with erythema multiforme. He was placed on intravenous steroids and H2 blockers. He was extubated 2 days later and discharged home 1 week after admission with a tapering dose of oral steroids and directions to follow-up with dermatology.

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**Figure 1.** (a) Oral mucosa involvement of rash showing erosions with hemorrhagic crust. (b) Multiple erythematous papules, plaques, and patches on the anterior chest and right shoulder.

## DISCUSSION

Erythema multiforme is a self-limited, hypersensitivity eruption of sharply demarcated papules and plaques, which can have the characteristic targetoid appearance and typically cover <10% of body surface area.<sup>1,6,7</sup> Many patients also exhibit mucosal involvement of the oral mucosa, conjunctiva, or genitals. Some experience burning or itching in the areas before lesions appear, but this is usually mild.<sup>6</sup> The histopathology of the lesion can range from edema in the papillary layer with minimal to no epidermal involvement, found in erythematous papular lesions, to extensive keratinocyte necrosis resulting in subdermal bullae formation, found in the classical target lesions.<sup>1</sup>

Despite its clinical similarities to Stevens-Johnson syndrome and the original thought it was part of a spectrum involving toxic epidermal necrolysis, erythema multiforme is now considered a separate entity.<sup>7</sup> A diagnosis of erythema multiforme was preferred over Stevens-Johnson syndrome in this case due to the patient's clinical presentation of several circular, symmetrically distributed, erythematous lesions, with some containing a slight central blister. While oral involvement is more commonly associated with Stevens-Johnson syndrome, oral mucosal lesions occur in >70% of cases of erythema multiforme and may be the only presenting sign with no concurrent skin lesions.<sup>7</sup>

Infectious causes of erythema multiforme are the most common and include herpes simplex virus, *Mycoplasma pneumoniae* (which usually occurs in children), hepatitis C, coxsackie virus, and Epstein-Barr virus.<sup>1</sup> Herpes simplex virus accounts for over 50% of cases and often causes recurrent episodes.<sup>6</sup> Mucocutaneous eruptions as a result of *M. pneumoniae*-induced rash and mucositis would present in a similar manner, but our patient tested negative for *M. pneumoniae*.<sup>8</sup> The second most common cause is drugs, including anticonvulsants, sulfonamides, penicillin, statins, nitrofurantoin, tetracyclines, and acetylsalicylic acid. Recently, there have been reports of tumor necrosis factor- $\alpha$  inhibitors such as adalimumab, infliximab, and etanercept as well as immunotherapy for melanoma and vaccinations causing an erythema multiforme reaction.<sup>1</sup> Rarely, have there been reports of herbicides causing erythema multiforme. Of the published reports, two cases involved an episode of irritant contact dermatitis prior to the eruption of targetoid lesions.<sup>4,5</sup> Our patient reported no rash before this presentation. There have been no case reports of atrazine as a cause of erythema multiforme.

Atrazine is a triazine drug, belonging to a class of nitrogen-containing heterocycles. It works by binding to plastoquinone-

binding protein in photosystem II, a protein that animals lack, and thereby inhibiting the electron transport process.<sup>9</sup> The plant dies as a result of photosynthesis inhibition.<sup>9</sup> A study to assess the percutaneous absorption of atrazine in human skin found that 16.4% of the applied dose was absorbed, indicating its permeability potential.<sup>10</sup> Many anticonvulsants also contain aromatic amine structures like atrazine and are well-known causes of erythema multiforme and Stevens-Johnson syndrome. Lamotrigine, phenytoin, and carbamazepine all contain aromatic amine groups, which have been more commonly related than others to the development of Stevens-Johnson syndrome and toxic epidermal necrolysis.<sup>11</sup> However, the relationship between the aromatic amine structure and the development of these hypersensitivity disorders is not understood.<sup>11</sup>

With so many known etiologies of erythema multiforme, it can be challenging to develop a good history and discover the cause for a hypersensitivity reaction. We present this case to highlight a previously unreported cause of erythema multiforme due to the chemical atrazine, found in Weed and Feed fertilizers.

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